In the Claims

Applicants have amended claims 19-24 in response to the Examiner's objections and rejections (see below). Applicants respond below to each of the Examiner's objections and rejections.

None of these amendments add new matter.

Claim Objections

Claims 19-22 and 24 stand objected to because of informalities in the claim language. Specifically, the Examiner contends that the terms "CnA" and "CnB" are unclear. The Examiner recommends at least one recitation of "calcineurin A" and "calcineurin B" for "CnA" and "CnB", respectively.

Applicants have obviated this objection by amending claim 19 to recite "calcineurin A" and by amending claim 21 to recite "calcineurin B."

Applicants acknowledge that the Examiner considers the abbreviations "FKBP12" and "FK506" to be sufficiently clear.

The Examiner further states that claim 21 recites the term "123" twice. Applicants have obviated the Examiner's objection by replacing the second recitation of

the term "123" with the term "124." Applicants have thereby corrected this inadvertent error. Support for this amendment is found at page 14, line 2 of the specification as originally filed.

The Rejections Under 35 U.S.C. § 112, Second Paragraph

Applicants acknowledge that the Examiner considers the incorporation by reference of Table 1 in claims 19-20 and 22-23 as proper.

Claims 19-24 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. The specific rejections are addressed individually below.

The Examiner has rejected claims 19-23 with respect to their use of the term "homologue." Specifically, the Examiner contends "that the term [homologue] is not defined by the specification or claims and may have several meanings in the art; e.g. structurally similar, physiological similar, of similar activity, etc." Applicants traverse.

The term "homologue" is defined in both the specification as originally filed (e.g. page 11, lines 14-17) and in original claims 19-23. Specifically, applicants disclose at page 11, lines 14-17 of the specification that a

homologue of said molecule or molecular complex comprises "a binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å." Thus, applicants have clearly defined the term "homologue" to encompass conformational or structural isomers whose backbone atoms fall within this root mean square deviation. Applicants therefore respectfully request that the Examiner withdraw these rejections.

The Examiner has rejected claims 19 and 21, contending that the recitation of the phrase "a binding pocket" in each step (a) of claims 19 and 21 is unclear. Specifically, the Examiner contends that "it is unclear whether the binding pocket of step (a) is intended to be the same as the binding pocket defined by the structure coordinates of lines 3-6 of claim 19 and lines 3-8 of claim 21, [and] is intended to be the same as the binding pocket of lines 8-10 of claim 19 and lines 10-12 of claim 21, or a different binding pocket than either of those recited earlier in the claims."

Applicants have obviated the Examiner's rejection by amending claims 19-20 to recite a "CnA binding pocket" and a "CnA homologue binding pocket." Claims 19 and 20, as amended, more clearly distinguish between a "CnA binding pocket" and a "CnA homologue binding pocket." Similarly,

applicants have amended claim 21 to recite a homologue that "comprises a CnA/CnB homologue binding pocket" (see, claim 21, lines 10-11). Applicants have also amended claim 22 to recite a homologue that "comprises a second homologue binding pocket" (see, claim 22, line 9).

The Examiner also states that the recitation of the phrase "the binding pocket" in each step (b) of claims 19 and 21 is unclear. Specifically, the Examiner contends that "[t]he antecedent basis for this term is unclear."

Applicants have obviated the Examiner's rejection by amending claims 19-20 to recite "the CnA binding pocket" and "CnA homologue binding pocket and claim 21 to recite "a CnA/CnB homologue binding pocket."

The Examiner has rejected claim 20 with respect to the recitation of the term "said binding pocket." Specifically, the Examiner contends that the antecedent basis for this term is unclear because claim 19, from which claim 20 depends, recites several binding pockets.

Applicants have obviated the Examiner's rejection by amending claim 20 to recite "said CnA binding pocket." The recitation of the term "said CnA binding pocket" in claim 20 has an antecedent basis in amended claim 19.

The Examiner has rejected claim 21, asserting that there is insufficient antecedent basis for "said amino

acids." Specifically, the Examiner states that it is unclear whether the antecedent basis for this term is CnA amino acids, CnB amino acids, or both.

Applicants have obviated the Examiner's rejection by amending claim 21 to clarify that the recited binding pocket is defined by both CnA and CnB amino acids. Applicants' amendment improves the claim language and defines the invention more clearly. Support for this amendment may be found throughout the specification as originally filed. Applicants have further amended claim 21 to recite the "the computational means to perform a fitting operation between the chemical entity and the CnA/CnB binding pocket or the CnA/CnB homologue binding pocket" to reflect the amendment.

The Examiner has rejected claim 22 for being indefinite. The Examiner contends that claim 22 limits claim 21 to a "second binding pocket" defined by certain structure coordinates. The Examiner further states that the CnA structure coordinates recited in claim 22 are identical to those recited for the CnA coordinates for the (first) binding pocket of claim 21, therefore it is unclear which structure coordinates claim 22 refers to. Applicants traverse.

Claim 22 is dependent from claim 19, not claim 21 as stated by the Examiner. The CnA structure coordinates for the second binding pocket as recited in claim 22 are

different than the structure coordinates for the first binding pocket as recited in claim 19. Therefore, claim 22 further limits claim 19 and depends properly from claim 19.

Applicants have also amended claim 22 to recite "said CnA and CnB amino acids" in line 10. Applicants' amendment improves the claim language and defines the invention more clearly. Support for this amendment may be found throughout the specification as originally filed.

The Examiner has rejected claim 23 with respect to the recitation of the phrase "the set of structure coordinates" in lines 2-3. Specifically, the Examiner states that the antecedent basis for the phrase "the set of structure coordinates" in claim 23 is unclear.

Applicants have obviated the Examiner's rejection by amending claim 23 to recite "a set of structure coordinates" in lines 2-3 of that claim. Claim 23, as amended, is directed to a method of evaluating the ability of a chemical entity to associate with a crystallized molecule or molecular complex, wherein said molecule or molecular complex is defined by a set of structure coordinates according to Figure 1.

The Examiner further contends that claim 23 is unclear as to the meaning of the phrase "set of structure coordinates." Applicants traverse.

Claim 23 refers to a "set of structure coordinates according to Figure 1." Applicants have clearly defined that the set of structure coordinates includes all coordinates depicted in Figure 1. Thus, applicants believe that claim 23 is not indefinite and respectfully request that the Examiner withdraw this rejection.

The Examiner has rejected claim 23, asserting that there is no antecedent basis for the recitation of "said amino acids."

Applicants have obviated the Examiner's rejection by amending claim 23 to recite "said CnA and CnB amino acids." Applicants' amendment improves the claim language and defines the amino acids more clearly.

The Examiner has rejected claim 24, asserting that the limitation "amino acids 17-392" is unclear. Specifically, the Examiner states that claim 24 is not commensurate in scope with the teachings of the specification, because claim 24 recites a molecule or molecular complex comprising amino acids 17-392 of CnA, CnB, FKBP12 and FK506, whereas the specification does not provide support for a combination of amino acids 17-392 of CnA, CnB, FKBP12 and FK506. Applicants disagree.

Throughout the specification as originally filed, applicants support the use of any portion of their structure coordinates.

Applicants have nevertheless obviated the Examiner's rejection by amending claim 24 to recite a "molecule or molecular complex comprises amino acids 17-392 of CnA, amino acids 1-169 of CnB, amino acids 1-107 of FKBP12 and FK506." Support for this amendment may be found at page 31, lines 8-13 and page 35, line 9 of the specification.

CONCLUSION

Based on the foregoing remarks, applicants request that the Examiner enter the above amendments and allow the claims to pass to issue.

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Signature of Person Signing

APPENDIX OF AMENDMENTS

19. A method for evaluating the ability of a chemical entity to associate with a crystallized molecule or molecular complex comprising a calcineurin A (CnA) binding pocket defined by structure coordinates of CnA amino acids 90, 91, 92, 118, 120, 121, 122, 150, 151, 156, 160, 199, 232, 253, 254, 256, 281, 282, 283, 284, 306, 311, 312, and 317 according to Figure 1, or a homologue of said molecule or molecular complex wherein said homologue comprises a CnA homologue binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å;

wherein said method comprises the steps of:

a. employing computational means to perform a fitting operation between the chemical entity and [a] the CnA binding pocket [of the molecule or molecular complex] or the CnA homologue binding pocket; and

b. analyzing the results of said fitting operation to quantify the association between the chemical entity and the CnA binding pocket or the CnA homologue binding pocket.

20. The method according to claim 19, wherein said CnA binding pocket is defined by structure coordinates of CnA

amino acids 90, 91, 92, 118, 120, 121, 122, 150, 151, 156, 160, 199, 281, 282, 283, 306, 311, 232, and 254, according to Figure 1, or a homologue of said molecule or molecular complex, wherein said homologue comprises a CnA homologue binding pocket that has a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å.

21. A method for evaluating the ability of a chemical entity to associate with a crystallized molecule or molecular complex comprising a CnA/CnB binding pocket defined by structure coordinates of CnA amino acids 122, 124, 159, 160, 310, 312, 313, 314, 339, 341, 343, 344, 345, 347, 351, 352, 353, 354, 355, 356, 359, 360, and 363; and [CnB] calcineurin B (CnB) amino acids 49, 50, 114, 115, 118, 119, 121, 122, 123, 124 [123], 157, 158, 159, 161, and 162 according to Figure 1, or a homologue of said molecule or molecular complex, wherein said homologue comprises a CnA/CnB homologue binding pocket that has a root mean square deviation from the backbone atoms of said CnA and CnB amino acids of not more than 1.5Å;

wherein said method comprises the steps of:

a. employing computational means to perform a fitting operation between the chemical entity and [a] the

CnA/CnB binding pocket [of the molecule or molecular complex] or the CnA/CnB homologue binding pocket; and

b. analyzing the results of said fitting operation to quantify the association between the chemical entity and the CnA/CnB binding pocket or the CnA/CnB homologue binding pocket.

22. The method according to claim 19, wherein said crystallized molecule or molecular complex further comprises a second binding pocket defined by CnA amino acids 122, 124, 159, 160, 310, 312, 313, 314, 339, 341, 343, 344, 345, 347, 351, 352, 353, 354, 355, 356, 359, 360, and 363; and CnB amino acids 49, 50, 114, 115, 118, 119, 121, 122, 123, 124, 157, 158, 159, 161, and 162; according to Figure 1, or a homologue of said molecule or molecular complex, wherein said homologue comprises a second homologue binding pocket that has a root mean square deviation from the backbone atoms of said CnA and CnB amino acids of not more than 1.5Å.

23. The method according to claim 22, wherein said molecule or molecular complex is defined by [the] a set of structure coordinates according to Figure 1, or a homologue thereof, wherein said homologue has a root mean square

deviation from the backbone atoms of said CnA and CnB amino acids of not more than 1.5Å.

24. The method according to claim 22, wherein said molecule or molecular complex comprises amino acids 17-392 of CnA, amino acids 1-169 of CnB, amino acids 1-107 of FKBP12 and FK506.